NOV 2 1 2013

1. SAFETY AND EFFECTIVENESS AS REQUIRED BY 21 CFR 807.92 STATEMENT

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirement 21 CFR 807.92.

2. SUBMITTER NAME AND ADDRESS

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3. 510k NUMBER, DEVICE PROPRIETARY NAME, COMMON NAME, PURPOSE FOR SUBMISSION, REGULATORY CLASSIFCATION, PANEL, PRODUCT CODE AND 21 CFR NUMBER

510k No: K123977

Device Proprietary Name: Randox Liquid CK-MB, Randox CK-MB Calibrator

Common Name: Liquid CK-MB, CK-MB Calibrator

Purpose for Submission: New Device

Regulatory Classification: Class II

Panel: Clinical Chemistry

21 CFR Number: 21 CFR 862.1215

4. PREDICATE DEVICE PROPRIETARY NAME AND 510 (k) NUMBER

Predicate Device Proprietary Name: Roche Diagnostics CK-MB reagent, Roche Diagnostics CK-MB calibrator for automated systems.

510 (k) Number: K003158

5. INTENDED USE

The CK-MB test system is a device intended for the quantitative in vitro determination of CK-MB concentration in serum and plasma. Measurements of CK-MB are used in the diagnosis and treatment of myocardial infarction (MI). This product is suitable for use on the RX series instruments including the RX Daytona and RX Imola. The Randox liquid CK-MB is for clinical laboratory use and not for point-of-care use.

The Randox CK-MB calibrator is an in vitro diagnostic product intended for use in the calibration of Randox CK-MB methods.

The Randox CK-MB control is an in vitro diagnostic product intended for use in the quality control of Randox CK-MB methods. This product was approved previously with the following 510(k) number: K951223

The Randox Tri-level Cardiac Controls is an in vitro diagnostic product intended for use in the quality control of Cardiac Markers on clinical chemistry and Immunoassay systems. This product was approved previously with the following 510(k) number: K041361

These in vitro diagnostic devices are intended for prescription use only and can only be used by professionals.

6. DEVICE DESCRIPTION

Liquid CK-MB is supplied in a kit containing:

- 4 x 20.0 mL CK-MB Buffer
- 4 x 6.0 mL CK-MB Substrate.

The CK-MB calibrator is lyophilised, single analyte, human serum based product. The kit contains ten vials (single level) with 1.0 mL per vial. Double de-ionised water is required for reconstitution.

7. PREDICATE DEVICE COMPARISON TABLE

Table 1 **Predicate Comparison**

CHARACTERISTICS	RANDOX LIQUID CK-MB	ROCHE DIAGNOSTIC SYSTEMS Inc. CK-MB REAGENT K003158
INTENDED USE	The CK-MB test system is a device intended for the quantitative in vitro determination of CK-MB concentration in serum and plasma. Measurements of CK-MB are used in the diagnosis and treatment of myocardial infarction (MI). This product is suitable for use on the RX series instruments including the RX Daytona and RX Imola..	The Roche Diagnostic Systems Inc. CK-MB reagent is an immunoinhibition assay for the quantitative in vitro determination of the MB isoenzyme of creatine kinase in human serum and plasma on Roche automated clinical chemistry analysers.
ASSAY PROTOCOL	Immunoinhibition Assay	UV assay with immunological inhibition of CK-M
FORMAT	Liquid which are ready to use	Liquids which are ready to use
KEY MATERIAL	Mouse anti-human CK-M monoclonal antibody	Mouse anti-human CK-M monoclonal antibody
STORAGE (unopened)	Reagents are stable up to the expiry date when stored unopened at +2 to +8°C	Reagents are stable up to the expiry date when stored unopened at +2 to +8°C
Sample Type	Plasma and serum	Plasma and serum
Sample Tubes	Heparin, EDTA	Heparin, EDTA
Control (Frequency)	-Randox CK-MB Control -Randox Tri-level Cardiac Controls levels 2 and 3 -Two levels of control should be assayed at least once a day	-Precinorm CK-MB Control -Precipath CK-MB -PreciControl ClinChem Multi 1 -Control interval per institution requirements

Table 1 **Predicate Comparison Continued.**

CHARACTERISTICS	RANDOX CK-MB CALIBRATOR	ROCHE DIAGNOSTIC SYSTEMS Inc. CK-MB CALIBRATOR K003158
INTENDED USE	The Randox CK-MB calibrator is an in vitro diagnostic product intended for use in the calibration of Randox CK-MB methods.	C.f.a.s (Calibrator for automated systems) CK-MB is for use in the calibration of Roche methods for the quantitative determination of CK-MB on Roche clinical chemistry analysers as specified in the value sheets.
ANALYTE	CK-MB	CK-MB
MATRIX	Human serum	Human serum
FORM	Lyophilised	Lyophilised
STORAGE (opened)	Stability of components in the reconstituted calibrator: At +25°C 8 hours At +4°C 5 days At -20°C 4 weeks when frozen once	Stability of components in the reconstituted calibrator: At 15-25°C 24 hours At 2-8°C 2 days At (-15)-(-25)°C 4 weeks when frozen once
(Unopened)	Stable to the expiration date at 2-8oC	Stable to the expiration date at 2-8oC

8. TEST PRINCIPLE [1]

Immunoinhibition Assay: An antibody is incorporated into the CK reagent. This antibody will bind to and inhibit the activity of the M subunit of CK-MB. This means that only the activity of the B subunit in serum is measured. If the activity is multiplied by a factor of 2, it will give the activity of CK-MB in serum.

(1) WURBURG, U., ET AL., CLIN. CHEM. 1976; 54: 357.

The R1 reagent contains anti CK-MM antibody which binds the M subunit of CK in the serum sample thereby inhibiting the activity of the CK- M subunit. The CK-B activity is determined by the CK NAC method.

$$\text{Creatine phosphate} + \text{ADP} \xrightarrow{CK} \text{Creatine} + \text{ATP}$$

$$\text{Glucose} + \text{ATP} \xrightarrow{HK} \text{Glucose-6-P} + \text{ADP}$$

$$\text{Glucose-6-P} + \text{NADP}^{+} \xrightarrow{\text{G-6-PDH}} \text{Gluconate-6-P} + \text{NADPH} + \text{H}^{+}$$

The rate of increase of absorbance at 340/700 nm due to the formation of NADPH is directly proportional to the activity of CK in the sample and if the activity is multiplied by a factor of two it will give the activity of CK-MB in the sample.

9. PERFORMANCE CHARACTERISTICS

Analytical performance:

a. Precision/Reproducibility:

Precision was evaluated consistent with C.L.S.I documents EP5 Precision studies were performed on the RX Daytona and RX Imola systems using control material and unaltered human serum samples that were spiked with CKMB concentrations of 10U/L, 50U/L, 250U/L, 450U/L and 1100U/L. Testing was conducted for one reagent lot of liquid CK-MB on one RX Daytona system and one RX Imola system, twice per day for 20 non-consecutive days. Two replicates per run was performed for each sample. No assay re-calibrations was required throughout the duration of the study. The results are summarized in the following tables.

Table 2 **CKMB RX Daytona Precision Summary**

All Data								Within Run		Between Run		Between Day		Total	
System	Method	Product	Data	# Day	# Run	# Rep	MEAN	SD	CV	SD	CV	SD	CV	SD	CV
Rx Daytona	CKMB	Human Serum 1	All	21	40	80	9.90	1.01	10.2	0.00	0.0	0.39	4.0	1.08	10.9
Rx Daytona	CKMB	Human Serum 5	All	21	40	80	1011.98	17.60	1.7	15.61	1.5	17.19	1.7	29.14	2.9
Rx Daytona	CKMB	Human Serum 3	All	21	40	80	244.85	4.29	1.8	2.70	1.1	3.34	1.4	6.07	2.5
Rx Daytona	CKMB	Human Serum 4	All	21	40	80	437.45	7.49	1.7	5.16	1.2	8.02	1.8	12.13	2.8
Rx Daytona	CKMB	Human Serum 2	All	21	40	80	47.53	1.00	2.1	0.78	1.6	0.89	1.9	1.55	3.3
Rx Daytona	CKMB	CKMB Calibrator	All	21	40	80	189.65	3.20	1.7	1.78	0.9	2.96	1.6	4.71	2.5
Rx Daytona	CKMB	CKMB control	All	21	40	80	137.45	2.79	2.0	3.11	2.3	1.43	1.0	4.42	3.2

Table 3 **CKMB RX Imola Precision Summary**

All Data								Within Run		Between Run		Between Day		Total	
System	Method	Product	Data	# Day	# Run	# Rep	MEAN	SD	CV	SD	CV	SD	CV	SD	CV
Rx Imola	CKMB	Human Serum 1	All	20	40	80	10.38	1.24	12.0	0.00	0.0	0.49	4.7	1.33	12.9
Rx Imola	CKMB	Human Serum 5	All	20	40	80	1001.29	18.07	1.8	33.15	3.3	14.51	1.4	40.45	4.0
Rx Imola	CKMB	Human Serum 3	All	20	40	80	245.62	4.84	2.0	3.98	1.6	5.54	2.3	8.36	3.4
Rx Imola	CKMB	Human Serum 4	All	20	40	80	437.83	8.51	1.9	6.23	1.4	9.98	2.3	14.52	3.3
Rx Imola	CKMB	Human Serum 2	All	20	40	80	47.43	1.53	3.2	1.42	3.0	1.12	2.4	2.37	5.0
Rx Imola	CKMB	CKMB Calibrator	All	20	40	80	186.69	5.05	2.7	0.00	0.0	3.46	1.9	6.12	3.3
Rx Imola	CKMB	CKMB control	All	20	40	80	135.57	3.70	2.7	0.39	0.3	0.39	0.3	3.74	2.8

b. Linearity/assay reportable range:

Linearity studies were performed to determine the analytical range of an assay - that is the range where the reported result is a linear function to the analyte concentration (or where deviation from linearity is less than 5%).

The linearity samples were prepared at 11 levels. The sponsor set a range from 0 analyte concentration (or other reasonable bottom of range level) up to a high concentration approximately 10% greater than the upper level of linearity to be claimed for the method. The results are summarized in the following table:

Table 4 **CKMB Linearity/ Reportable Range Summary**

CKMB	Linearity	Reportable Range
RX Daytona	2000 U/L	7 – 2000U/L
RX Imola	1100 U/L	6 – 1100U/L

Table 5 **CKMB Validated Extended Recovery**

CKMB	Extended Recovery on event of Re-run
RX Daytona	10200 U/L ± 10%
RX Imola	10200 U/L ± 10%

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Table 6 **Traceability Table Randox Liquid CK-MB Reagent and CK-MB Calibrator**

Product	Analyte	Supplier	Product No	Origin	Source
CK-MB Calibrator	CK-MB	Lee Biosolutions	190-24	Human	Human Heart
Liquid CK-MB	CK-MB	Roche	04688457	Animal	Mouse

d. Detection limit:

Sensitivity studies have been carried out in accordance with C.L.S.I. guideline EP17-A 'Protocols for Determination of Limits of Detection and Limits of Quantification; Approved Guideline'. A Limit of Blank (L.o.B.), a Limit of Detection (L.o.D.) and a Limit of Quantification were performed on the RX Daytona and RX Imola systems.

CKMB on the RX Daytona

The Limit of Detection (LoD) for CKMB on the RX Daytona is 5.06 U/L based on 300 determinations, with 1 blank and 4 low level samples.

The Limit of Blank (LoB) is 2.91 U/L.

The Limit of Quantitation (LoQ) is 7.00 U/L as determined by the lowest concentration at which precision and accuracy are still met. Acceptable criteria ≤20% accuracy and ≤20% imprecision.

CKMB on the RX Imola

The Limit of Detection (LoD) for CKMB on the RX Imola is 2.41 U/L based on 300 determinations, with 1 blank and 4 low level samples.

The Limit of Blank (LoB) is 0.87 U/L.

The Limit of Quantitation (LoQ) is 6.00 U/L as determined by the lowest concentration at which precision and accuracy are still met. Acceptable criteria ≤20% accuracy and ≤20% imprecision.

e. Analytical Specificity:

The effects of potential interferents were determined by calculating the mean value of the spiked interferent with the corresponding control solution. Potential interferents and some commonly used drugs and exogenous susbstances were spiked into two serum pools with a CK-MB concentration of approximately 20U/L and 415U/L. The spiked sample results were compared to control samples prepared without the potential interferents.

Acceptance Criteria: % of Control ± 10%

The results are summarized in the following table. No interference was observed at the concentrations listed in the table.

Table 7 **CKMB Interference Summary**

	RX daytona	RX imola
Interferent	**CKMB Low Pool**	**CKMB Low Pool**
Haemoglobin	1000 mg/dl	1000 mg/dl
Bilirubin (F)	30 mg/dl	30 mg/dl
Bilirubin (C)	60 mg/dl	60 mg/dl
Intralipid ®	Inteferes*	Inteferes *
Triglycerides	500 mg/dl	500 mg/dl
Acetominophen	1660µmol/l	1660µmol/l
Caffeine	308µmol/l	308µmol/l
Phenytoin	198µmol/l	198µmol/l
Salicyclic Acid	4.34µmol/l	4.34µmol/l
Digoxin	6.15µmol/l	6.15µmol/l
Nicotine	6.2µmol/l	6.2µmol/l
Theophylline	222µmol/l	222µmol/l
Acetyl Salicyclic Acid	3333µmol/l	3333µmol/l
Ascorbic Acid	227µmol/l	227µmol/l
Chloramphenicol	155µmol/l	155µmol/l
Furosemide	181µmol/l	181µmol/l
Ibuprofen	2425µmol/l	2425µmol/l

***Recommend the use of clear, non-lipemic serum and plasma**

Comparison Studies:

a. Method comparison with predicate device:

Correlation studies were carried out in accordance with C.L.S.I. guideline EP9-A2 'Method Comparison and Bias Estimation Using Patient Samples: Approved Guideline – Second Edition'.

90 serum samples (6 spikes) were tested on the RX Daytona analyzer and 93 serum samples (4 spikes) were tested on the RX Imola across 5 working days with each sample tested in singlicate. The test method was compared to the predicate device Roche CKMB Kit (ref. 12132893) that was tested on the Hitachi 717. One RX Daytona, one RX Imola and one Hitachi 717 system were used to carry out the testing.

The results of the studies are shown below.

CKMB on the RX Daytona v the predicate device

This method (Y) was compared with another commercially available method (X).
90 serum patient samples were analyzed spanning the range 8.88 to 1931.75 U/L and the following linear regression equation was obtained:

Y = 0.95 + 0.59

Correlation coefficient of r = 0.999

CKMB on the RX Imola v the predicate device

This method (Y) was compared with another commercially available method (X).
93 serum patient samples were analyzed spanning the range 6.64 to 992.31 U/L and the following linear regression equation was obtained:

Y = 0.96 + 2.36

Correlation coefficient of r = 0.999

b. Matrix comparison:

Matrix method comparisons for the CKMB assay on the RX Daytona and RX Imola systems were assessed. Both serum, lithium heparin and potassium EDTA plasma were conducted to determine whether method accuracy with lithium heparin and potassium EDTA plasma specimens are equivalent to serum results and that lithium heparin and potassium EDTA plasma does not interfere with either the method or the system.

CKMB Matrix comparison on the RX Daytona (Lithium Heparin)

Patient samples were drawn in matched pairs – one sample serum (x) and the second sample lithium heparin plasma (y). A minimum of 72 matched patient sample pairs were analyzed spanning the range 9.09 to 1931.8U/L and the following linear regression equation was obtained:

Y = 1.01x + -0.19

Correlation coefficient of r = 1.000

CKMB Matrix comparison on the RX Daytona (Potassium EDTA)

Patient samples were drawn in matched pairs – one sample serum (x) and the second sample potassium EDTA plasma (y). A minimum of 71 matched patient sample pairs were analyzed spanning the range 9.09 to 1931.9 U/L and the following linear regression equation was obtained:

Y = 1.03x -1.92

Correlation coefficient of r = 0.999

CKMB Matrix comparison on the RX Imola (Lithium Heparin)

Patient samples were drawn in matched pairs – one sample serum (x) and the second sample lithium heparin plasma (y). A minimum of 71 matched patient sample pairs were analyzed spanning the range 6.81 to 992.31U/L and the following linear regression equation was obtained:

Y = 1.00x + 0.37

Correlation coefficient of r = 0.999

CKMB Matrix comparison on the RX Imola (Potassium EDTA)

Patient samples were drawn in matched pairs – one sample serum (x) and the second sample potassium EDTA plasma (y). A minimum of 71matched patient sample pairs were analyzed spanning the range 6.64 to 992.31 U/L and the following linear regression equation was obtained:

Y = 1.01x + 0.90

Correlation coefficient of r = 1.000

Clinical studies:

a. Clinical Sensitivity

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

Clinical cut-off:

Not applicable

Expected values/Reference range:

The Reference range was evaluated consistent with C.L.S.I guideline C28-A2, How to Define and Determine Reference Intervals in the Clinical Laboratory. In a study, human serum from 40 normal donors (16 Male, 24 Female with age ranging from 17 to 69) were tested in singlicate on both the RX imola and RX daytona. The results obtained from both systems were ordered from lowest to highest before being examined for outliers using the Dixon test.

The following references have been cited on the package insert:

Klein G, Berger A, Bertholf R et al. Abstract: Multicenter Evaluation of Liquid Reagents for CK, CK-MB and LDH with Determination of Reference Intervals on Hitachi Systems. Clin Chem 2001; 47:Suppl. A30.

Thomas L, Müller M, Schumann G, Weidemann G et al. Consensus of DGKL and VDGH for interim reference intervals on enzymes in serum. J Lab Med 2005;29:301-308.

Upon confirmation there were no outliers in either data set, the values were compared to the quoted range of CK-MB <25U/L. Results of the study indicate that all values reported in the range for Healthy Individuals.

10. CONCLUSION

Testing results indicate that the proposed device is safe and effective for the stated intended use and is substantially equivalent to the predicate devices.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

November 21, 2013

RANDOX LABORATORIES, LTD.
DR. PAULINE ARMSTRONG
55 DIAMOND RD.
CRUMLIN, COUNTY ANTRIM BT29 4QY
UK

Re: K123977
Trade/Device Name: Randox Liquid CK-MB, Randox CK-MB Calibrator
Regulation Number: 21 CFR 862.1215
Regulation Name: Creatine phosphokinase/creatine kinase or isoenzymes test system
Regulatory Class: II
Product Code: CGS, JIT
Dated: November 13, 2013
Received: November 18, 2013

Dear Dr. Armstrong:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol C. Benson -S for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K123977

Device Name
Randox Liquid CK-MB, Randox CK-MB Calibrator

Indications for Use *(Describe)*

Randox Liquid CK-MB
The Randox Liquid CK-MB test system is a device intended for the quantitative in vitro determination of CK-MB concentration in serum and plasma. Measurements of CK-MB are used in the diagnosis and treatment of myocardial infarction (MI). This product is suitable for use on the RX series instruments including the RX Daytona and the RX Imola.

Randox CK-MB Calibrator
The Randox CK-MB calibrator is an in vitro diagnostic product intended for use in the calibration of Randox CK-MB methods

The Randox Liquid CK-MB test system for the RX Imola and RX Daytona is a prescription use device intended to be used in clinical laboratories only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Ruth A. Chesler -S